```
=> fil reg; d que l3
FILE 'REGISTRY' ENTERED AT 12:58:20 ON 09 AUG 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    8 AUG 2004  HIGHEST RN 724421-42-5
DICTIONARY FILE UPDATES:   8 AUG 2004  HIGHEST RN 724421-42-5

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html


L3             4 SEA FILE=REGISTRY ABB=ON  ^KDEL^/SQSP


=> d rn cn sql kwic nte lc l3 1-4

L3   ANSWER 1 OF 4  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   263749-13-9  REGISTRY
CN   L-Leucine, N2-[[5-hydroxy-2-(1-naphthalenyl)-4-oxazolyl]methylene]-L-lysyl-
     L-.alpha.-aspartyl-L-.alpha.-glutamyl- (9CI)  (CA INDEX NAME)
SQL  4

SEQ      1 KDEL
           ====
HITS AT:   1-4

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
NTE  modified (modifications unspecified)
-----------------------------------------------------------------------
 type            ------ location ------         description
-----------------------------------------------------------------------
modification     Lys-1           -         undetermined modification
-----------------------------------------------------------------------
LC   STN Files:   CA, CAPLUS

L3   ANSWER 2 OF 4  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   221896-52-2  REGISTRY
CN   L-Leucine, N2-(bromoacetyl)-L-lysyl-L-.alpha.-aspartyl-L-.alpha.-glutamyl-
     (9CI)  (CA INDEX NAME)
SQL  4

SEQ      1 KDEL
           ====
HITS AT:   1-4

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
NTE  modified (modifications unspecified)
-----------------------------------------------------------------------
```

type	------ location ------		description
modification	Lys-1	-	bromoacetyl<Bac>

LC STN Files: CA, CAPLUS

L3 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2004 ACS on STN
RN 217658-09-8 REGISTRY
CN D-Leucine, D-lysyl-D-.alpha.-aspartyl-D-.alpha.-glutamyl- (9CI) (CA INDEX NAME)
SQL 4

SEQ 1 KDEL
====
HITS AT: 1-4

RELATED SEQUENCES AVAILABLE WITH SEQLINK
LC STN Files: CA, CAPLUS

L3 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2004 ACS on STN
RN 113516-56-6 REGISTRY
CN L-Leucine, L-lysyl-L-.alpha.-aspartyl-L-.alpha.-glutamyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 10: PN: WO0175132 SEQID: 9 unclaimed sequence
CN 10: PN: WO0210187 SEQID: 10 unclaimed sequence
CN 10: PN: WO03052117 SEQID: 10 unclaimed sequence
CN 118: PN: US6037329 SEQID: 42 unclaimed protein
CN 11: PN: US20030167531 SEQID: 9 unclaimed sequence
CN 11: PN: WO2004050849 SEQID: 11 unclaimed sequence
CN 127: PN: US6506379 SEQID: 2 unclaimed sequence
CN 12: PN: WO2004044141 SEQID: 18 unclaimed sequence
CN 13: PN: DE19933492 PAGE: 6 claimed protein
CN 14: PN: JP2003334080 SEQID: 17 unclaimed protein
CN 14: PN: WO0242325 SEQID: 15 unclaimed sequence
CN 152: PN: US6696061 SEQID: 152 unclaimed sequence
CN 157: PN: US20030143562 SEQID: 157 unclaimed sequence
CN 159: PN: US20030224412 SEQID: 157 unclaimed sequence
CN 15: PN: WO2004053499 SEQID: 34 unclaimed sequence
CN 16: PN: WO0160393 SEQID: 16 unclaimed sequence
CN 16: PN: WO2004013330 SEQID: 16 unclaimed sequence
CN 17: PN: WO0142211 SEQID: 93 unclaimed sequence
CN 18: PN: WO02060935 SEQID: 23 unclaimed sequence
CN 18: PN: WO02097120 SEQID: 15 unclaimed sequence
CN 1: PN: CN1382734 PAGE: 1 claimed sequence
CN 1: PN: WO0105936 PAGE: 10 unclaimed sequence
CN 1: PN: WO0179259 SEQID: 1 unclaimed sequence
CN 1: PN: WO0207775 SEQID: 1 claimed protein
CN 1: PN: WO02093177 PAGE: 95 claimed protein
CN 1: PN: WO0244720 SEQID: 2 unclaimed sequence
CN 1: PN: WO03065012 SEQID: 1 claimed sequence
CN 1: PN: WO9966026 SEQID: 2 claimed protein
CN 21: PN: WO9966959 SEQID: 19 claimed protein
CN 22: PN: US20020157120 SEQID: 22 unclaimed
CN 22: PN: WO0041474 SEQID: 8 unclaimed protein
CN 22: PN: WO0071565 SEQID: 22 unclaimed sequence
CN 23: PN: JP2002253262 SEQID: 23 unclaimed sequence
CN 23: PN: US20030135887 PAGE: 30 claimed sequence
CN 23: PN: US6194560 SEQID: 24 unclaimed sequence para q
CN 23: PN: WO03068941 SEQID: 23 unclaimed sequence
CN 25: PN: US6183746 SEQID: 23 unclaimed sequence ok
CN 25: PN: US6562800 SEQID: 23 claimed sequence

```
CN   25: PN: WO0015651 SEQID: 17 unclaimed protein
CN   25: PN: WO0118208 PAGE: 23 unclaimed sequence
CN   25: PN: WO02062822 SEQID: 25 unclaimed sequence
CN   26: PN: US20040071696 SEQID: 26 unclaimed sequence
CN   26: PN: WO03020896 SEQID: 30 unclaimed sequence
CN   26: PN: WO03054164 SEQID: 26 unclaimed sequence
CN   27: PN: US20030162733 PAGE: 46 claimed sequence
CN   27: PN: WO02068453 SEQID: 83 unclaimed sequence
CN   28: PN: US6280937 SEQID: 27 unclaimed sequence
CN   28: PN: US6455247 SEQID: 28 unclaimed sequence
CN   29: PN: US20020001830 SEQID: 29 unclaimed sequence
CN   2: PN: WO0077174 SEQID: 2 unclaimed sequence
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for
     DISPLAY
SQL  4

SEQ      1 KDEL
           ====
HITS AT:   1-4

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
LC   STN Files:   CA, CANCERLIT, CAPLUS, CHEMCATS, MEDLINE, TOXCENTER, USPAT2,
       USPATFULL


=> d his l10-

     (FILE 'CAPLUS, USPATFULL, MEDLINE, CANCERLIT, TOXCENTER' ENTERED AT
     13:01:02 ON 09 AUG 2004)
L10            1 S L6
L11            1 S L7
L12            1 S L8
L13          440 S L9

=> s l10 or l11 or l12
L14            3 L10 OR L11 OR L12   - hits for the first 3 Registry numbers

=> dup rem l14
PROCESSING COMPLETED FOR L14
L15            3 DUP REM L14 (0 DUPLICATES REMOVED)
                 ANSWERS '1-3' FROM FILE CAPLUS

=> d ibib ed ab hitrn l15 1-3

L15  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:          2000:44913  CAPLUS
DOCUMENT NUMBER:           132:279508
TITLE:                     Solid phase synthesis of KDEL peptides labeled with
                           fluorophore and/or bifunctional chelating agent for
                           receptor localization
AUTHOR(S):                 Nagy, Ildiko B.; Mak, Marianna; Varga, Imre; Kovacs,
                           Janos; Fellinger, Erzsebet; Hudecz, Ferenc
CORPORATE SOURCE:          Research Group of Peptide Chemistry, Hungarian Academy
                           of Sciences, Budapest, H-1518, Hung.
SOURCE:                    Innovation and Perspectives in Solid Phase Synthesis &
                           Combinatorial Libraries: Peptides, Proteins and
                           Nucleic Acids--Small Molecule Organic Chemical
                           Diversity, Collected Papers, International Symposium,
                           5th, London, Sept. 2-6, 1997 (1999), Meeting Date
                           1997, 229-230.  Editor(s): Epton, Roger.  Mayflower
                           Scientific Ltd.: Kingswinford, UK.
                           CODEN: 68OEAA
```

DOCUMENT TYPE: Conference
LANGUAGE: English
ED Entered STN: 19 Jan 2000
AB A symposium report. KDEL peptides were labeled with a fluorophore, 4-ethoxymethylene-2(1)-naphthyl-5(4H)-oxazolone, and/or with a bifunctional chelating agent, diethylenetriaminepentaacetic acid anhydride, at unprotected .alpha.- and/or .epsilon.-amino groups.
IT **263749-13-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid-phase synthesis of KDEL peptides labeled with fluorophores and/or bifunctional chelating agents useful for receptor localization studies)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:49844 CAPLUS
DOCUMENT NUMBER: 130:264341
TITLE: Optimized Conditions to Couple Two Water-Soluble Biomolecules through Alkylamine Thiolation and Thioetherification
AUTHOR(S): Meunier, Laurent; Bourgerie, Sylvain; Mayer, Roger; Roche, Annie-Claude; Monsigny, Michel
CORPORATE SOURCE: Glycobiologie Centre de Biophysique Moleculaire, CNRS, Orleans, 45071, Fr.
SOURCE: Bioconjugate Chemistry (1999), 10(2), 206-212
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 26 Jan 1999
AB A simple method for introducing, in buffered saline, a reactive sulfhydryl group on water-sol. mols. bearing an alkyl-amino group is described. This method is based on the use of two water-sol. reagents: 2-iminothiolane and 6,6'-dithiodinicotinic acid. The first one is open upon reaction with an amino group, and the generated thiol group is immediately protected by action of the second reagent. The optimal conditions were detd. by taking into account the stability and the reactivity of both reagents with regards to pH and temp. This method was validated through two applications, the substitution of bovine serum albumin with a bromoacetyl peptide and the substitution of an amino link at the 5' end of an oligonucleotide by reaction with either a fluorescent tag, iodoacetamidofluorescein, or a bromoacetyl peptide, upon redn. of the protected disulfide bridge with a third water-sol. reagent, namely tris(2-carboxyethyl)phosphine.
IT **221896-52-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(optimized conditions to couple two water-sol. peptides or oligonucleotides through alkylamine thiolation and thioetherification)
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:676027 CAPLUS
DOCUMENT NUMBER: 130:63194
TITLE: Diffusion Edited NMR: Screening Compound Mixtures by Affinity NMR to Detect Binding Ligands to Vancomycin
AUTHOR(S): Bleicher, Konrad; Lin, Mengfen; Shapiro, Michael J.; Wareing, James R.
CORPORATE SOURCE: Department of Metabolic and Cardiovascular Diseases Preclinical Research, Novartis Pharmaceuticals Corporation, Summit, NJ, 07901, USA

SOURCE: Journal of Organic Chemistry (1998), 63(23), 8486-8490
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 27 Oct 1998
AB Affinity NMR can be used to produce an edited NMR spectrum that identifies ligands that bind to vancomycin from soln. mixts. contg. nonbinding mols. The Diffusion EnCODEd Spectroscopy (DECODES) expt. performed directly on the same sample can be used to det. the structure of the binding ligands without the need for a phys. sepn. step. The all-D amino acid tetrapeptides DDFA and DDFS, known ligands for vancomycin, were identified in the presence of eight nonbinding tetrapeptides. The bound-ligand signals in the two-dimensional DECODES spectrum are readily identified by comparison with the spectral patterns of the vancomycin cross-peaks in the 2D total correlation spectroscopy and correlation spectroscopy spectra. The screening of soln. mixts. of mols. for direct detection of mol. interactions and structural identification of the interacting ligands provides a powerful new tool to complement methods, such as affinity MS, which rely on the phys. sepn. of mixt. components to identify mol. interactions. The soln. mixts. of compds. for screening by affinity NMR could come from any source where the components are in similar relative amts., including synthesis by combinatorial chem. methods.
IT **217658-09-8**
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(diffusion edited NMR screening of ligand binding to vancomycin)
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s l13 not l15
L16 439 L13 NOT (L15) printed above The 4th Registry number had many hits

=> dup rem l16
PROCESSING COMPLETED FOR L16
L17 299 DUP REM L16 (140 DUPLICATES REMOVED)
ANSWERS '1-138' FROM FILE CAPLUS
ANSWERS '139-224' FROM FILE USPATFULL
ANSWERS '225-294' FROM FILE MEDLINE
ANSWER '295' FROM FILE CANCERLIT
ANSWERS '296-299' FROM FILE TOXCENTER

=> sort l17 py a
SORT ENTIRE ANSWER SET? (Y)/N:y
PROCESSING COMPLETED FOR L17
L18 299 SORT L17 PY A sorted answer set & printed 30 oldest references

=> d ibib ed ab hitrn l18 1-30; fil hom

L18 ANSWER 1 OF 299 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1988:126931 CAPLUS
DOCUMENT NUMBER: 108:126931
TITLE: A C-terminal signal prevents secretion of luminal ER proteins
AUTHOR(S): Munro, Sean; Pelham, Hugh R. B.
CORPORATE SOURCE: MRC Lab. Mol. Biol., Cambridge, CB2 2QH, UK
SOURCE: Cell (Cambridge, MA, United States) (1987), 48(5), 899-907
CODEN: CELLB5; ISSN: 0092-8674
DOCUMENT TYPE: Journal

LANGUAGE: English
ED Entered STN: 15 Apr 1988
AB Proteins that permanently reside in the lumen of the endoplasmic reticulum (ER) must somehow be distinguished from newly synthesized secretory proteins, which pass through this compartment of their way out of the cell. Three luminal ER proteins whose sequence is known, grp78 (BiP), grp94, and protein disulfide isomerase, share the C-terminal sequence Lys-Asp-Glu-Leu (KDEL). Deletion (or extension) of the C-terminus of grp78 resulted in secretion of this protein when it was expressed in COS cells. Conversely, a deriv. of chicken lysozyme contg. the last 6 amino acids of grp78 failed to be secreted and instead accumulated in the ER. The KDEL sequence may mark proteins that are to be retained in the ER; possible retention mechanisms are discussed.
IT **113516-56-6**
RL: BIOL (Biological study)
(protein secretion from luminal endoplasmic reticulum inhibition by)

L18 ANSWER 2 OF 299 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:96250 CAPLUS
DOCUMENT NUMBER: 114:96250
TITLE: Cytotoxic recombinant Pseudomonas endotoxin and target-specific fusion products
INVENTOR(S): Pastan, I.
PATENT ASSIGNEE(S): National Institutes of Health, USA
SOURCE: U. S. Pat. Appl., 33 pp. Avail. NTIS Order No. PAT-APPL-7-759 635.
CODEN: XAXXAV
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 459635	A0	19900415	US 1990-459635	19900102
US 522563	A0	19910515	US 1990-522563	19900514
US 5458878	A	19951017		
CA 2072891	AA	19910703	CA 1990-2072891	19901227
CA 2072891	C	19991221		
WO 9109949	A1	19910711	WO 1990-US7421	19901227
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
AU 9172424	A1	19910724	AU 1991-72424	19901227
AU 644139	B2	19931202		
EP 509056	A1	19921021	EP 1991-904103	19901227
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05502032	T2	19930415	JP 1991-504333	19911217
US 5705163	A	19980106	US 1995-461233	19950605
PRIORITY APPLN. INFO.:			US 1990-459635	19900102
			US 1990-522563 A3	19900514
			WO 1990-US7421 A	19901227

ED Entered STN: 23 Mar 1991
AB The carboxyl terminus of Pseudomonas exotoxin A (PE), residues Arg609-Lys613, dets. the cytotoxic activity of the exotoxin. Peptide sequence Lys-Asp-Glu-Leu (KDEL), which is responsible for retaining newly formed proteins within the endoplasmic reticulum, has similar biol. function to the carboxyl terminus of PE. When KDEL is fused to a carboxyl terminus-deleted PE mutant (non-cytotoxic), it restored the cytotoxic activity of the toxin. A recognition mol. such as antibody may be fused to the carboxyl terminus of PE to increase the potency of the chimeric toxin. Fusion proteins of PE and transforming growth factor .alpha. were prepd., and their cytotoxic activity against Swiss 3T3 cells detd. The

fusion proteins with active carboxyl terminus were .gtoreq.50 fold more cytotoxic than that contg. inactive PE carboxyl terminus.

IT **113516-56-6**
RL: PRP (Properties)
(exotoxin A carboxyl-terminus of Pseudomonas contg., retention of toxin in endoplasmic reticulum and cytotoxicity in relation to)

L18 ANSWER 3 OF 299 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:59407 CAPLUS
DOCUMENT NUMBER: 114:59407
TITLE: C-terminal KDEL-modified cystatin C is retained in transfected CHO cells
AUTHOR(S): Johansen, Teit Eliot; Vogel, Charlotte K.; Schwartz, Thue W.
CORPORATE SOURCE: Univ. Dep. Clin. Chem., Rigshosp., Copenhagen, DK-2100, Den.
SOURCE: Biochemical and Biophysical Research Communications (1990), 172(3), 1384-91
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 23 Feb 1991
AB The significance of a C-terminal tetrapeptide, Lys-Asp-Glu-Leu (KDEL), as a retention signal for the endoplasmic reticulum was studied using cystatin C, a general thiol protease inhibitor, as the reporter protein. Clones of CHO cells were analyzed after stable transfection with eukaryotic expression vectors encoding either cystatin C, KDEL-extended cystatin C, or cystatin C extended with a control sequence. Cystatin C with the KDEL tetrapeptide as a C-terminal extension is retained intracellularly without apparent accumulation of the mol.
IT **113516-56-6**
RL: BIOL (Biological study)
(as C-terminal retention signal, cystatin C retention in endoplasmic reticulum mediation by)

L18 ANSWER 4 OF 299 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:512802 CAPLUS
DOCUMENT NUMBER: 113:112802
TITLE: Identification by anti-idiotype antibodies of an intracellular membrane protein that recognizes a mammalian endoplasmic reticulum retention signal
AUTHOR(S): Vaux, David; Tooze, John; Fuller, Stephen
CORPORATE SOURCE: Cell Biol. Programme, Eur. Mol. Biol. Lab., Heidelberg, 6900, Germany
SOURCE: Nature (London, United Kingdom) (1990), 345(6275), 495-502
CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 29 Sep 1990
AB Monoclonal antibodies were raised against antibodies to distinct carboxy-terminal KDEL sequences of two sol., resident endoplasmic reticulum proteins. These anti-idiotype reagents recognize an intrinsic membrane protein with characteristics expected of a receptor responsible for the recognition and return of resident proteins to the endoplasmic reticulum.
IT **113516-56-6**
RL: BIOL (Biological study)
(endoplasmic reticulum-resident proteins contg., receptor for, antiidiotypic antibody detection of, in salvage compartment)

L18 ANSWER 5 OF 299 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1991:555684 CAPLUS
DOCUMENT NUMBER: 115:155684
TITLE: Characterization of the carboxyl-terminal sequences responsible for protein retention in the endoplasmic reticulum
AUTHOR(S): Andres, Douglas A.; Rhodes, Janette D.; Meisel, Robert L.; Dixon, Jack E.
CORPORATE SOURCE: Dep. Biochem., Purdue Univ., West Lafayette, IN, 47907, USA
SOURCE: Journal of Biological Chemistry (1991), 266(22), 14277-82
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 18 Oct 1991
AB The C-terminal sequence KDEL has been shown to be essential for the retention of several proteins in the lumen of the endoplasmic reticulum. It was previously demonstrated that variants to the KDEL retention signal, particularly at the initial 2 positions of the tetrapeptide, can be made without affecting its ability to direct intracellular retention when appended to the neuropeptide Y precursor (pro-NPY). To further investigate the nature of the KDEL retention signal, oligonucleotide-directed mutagenesis and transfection was used to generate stable mouse anterior pituitary AtT-20 cell lines expressing pro-NPY mutants with variants of the KDEL sequence added to their direct C-terminus. Analyses of dibasic processing and indirect immunofluorescent microscopy of AtT-20 subclones were consistent with the retention of the pro-NPY mutants bearing the C-terminal extensions QDEL, KEDL, or KEDI within the endoplasmic reticulum. A change in the final amino acid of the tetrapeptide from Leu to Val abolished retention completely, and the peptide hormone was processed and secreted. These results indicate that only a limited no. of conservative changes can be made to the final 2 positions of the tetrapeptide without abolishing activity and suggest a highly specific interaction of the retention signal and the KDEL receptor.
IT **113516-56-6**
RL: BIOL (Biological study)
(as protein retention signal, in endoplasmic reticulum, structure in relation to)

L18 ANSWER 6 OF 299 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:77625 CAPLUS
DOCUMENT NUMBER: 118:77625
TITLE: Identification by anti-idiotype antibodies of an intracellular membrane protein that recognizes a mammalian endoplasmic reticulum retention signal. [Retraction to document cited in CA113(13):112802w]
AUTHOR(S): Vaux, David; Tooze, John; Fuller, Stephen
CORPORATE SOURCE: Cell Biol. Programme, Eur. Mol. Biol. Lab., Heidelberg, 6900, Germany
SOURCE: Nature (London, United Kingdom) (1992), 360(6402), 372
CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 02 Mar 1993
AB Data in Fig. 2 was erroneous. The authors request retraction of the statement that the 72K protein is an integral membrane protein and of speculation concerning its function.
IT **113516-56-6**
RL: BIOL (Biological study)
(endoplasmic reticulum-resident proteins contg., receptor for, antiidiotypic antibody detection of, in salvage compartment (Retraction))

L18 ANSWER 7 OF 299 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1992:211650 CAPLUS
DOCUMENT NUMBER: 116:211650
TITLE: Retention of a type II surface membrane protein in the endoplasmic reticulum by the Lys-Asp-Glu-Leu sequence
AUTHOR(S): Tang, Bor Luen; Wong, Siew Heng; Low, Seng Hui; Hong, Wanjin
CORPORATE SOURCE: Inst. Mol. Cell Biol., Natl. Univ. Singapore, Singapore, 0511, Singapore
SOURCE: Journal of Biological Chemistry (1992), 267(10), 7072-6
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 31 May 1992
AB Sol. luminal proteins of the endoplasmic reticulum (ER) are known to be retained by a tetrapeptide retention signal, KDEL. The KDEL sequence when appended to the C-terminus of a cell surface membrane protein, dipeptidylpeptidase IV (DPPIV), resulted in its retention in the endoplasmic reticulum of transfected MDCK cells as assessed by indirect immunofluorescence. Selective surface biotinylation revealed that .apprx.90-95% of the expressed DPPIV was retained in the ER. Appendance of the sequence KDEV did not, however, result in ER retention, illustrating the functional specificity of the retention signal. The ER retention was not due to misfolding of the mutant protein, as the mutant proteins remained enzymically active. The data suggest that the KDEL receptor is able to recognize and recycle type II membrane proteins contg. a C-terminal KDEL sequence and postulated the existence of such yet to be identified endogenous proteins.
IT **113516-56-6**
RL: BIOL (Biological study)
(as signal peptide for dipeptidyl peptidase IV retention in endoplasmic reticulum)

L18 ANSWER 8 OF 299 MEDLINE on STN
ACCESSION NUMBER: 93016328 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1383243
TITLE: Immunological evidence that plants use both HDEL and KDEL for targeting proteins to the endoplasmic reticulum.
AUTHOR: Napier R M; Fowke L C; Hawes C; Lewis M; Pelham H R
CORPORATE SOURCE: Horticulture Research International, West Malling, Kent, UK.
SOURCE: Journal of cell science, (1992 Jun) 102 (Pt 2) 261-71.
Journal code: 0052457. ISSN: 0021-9533.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199211
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19960129
Entered Medline: 19921123
ED Entered STN: 19930122
Last Updated on STN: 19960129
Entered Medline: 19921123
AB The epitopes of two monoclonal antibodies raised to a putative auxin receptor have been mapped. Carboxy-peptidase A digestion of the antigen, auxin-binding protein (ABP) purified from maize, completely abolished binding of antibody MAC 256 and impaired binding of MAC 259, suggesting that they both recognise C-terminal epitopes. Published sequences of ABP showed that the C terminus was KDEL, a tetrapeptide used for targeting

proteins to the ER in animal cells. We have used this short homology to confirm that the two monoclonals recognise C-terminal KDEL, showing that animal KDEL proteins and synthetic KDEL peptides are recognised and that animal cell ER is stained strongly and specifically. Sucrose density gradient fractionation of maize microsomal membranes showed that plant KDEL proteins, including ABP, fractionated with markers for the endoplasmic reticulum. However, few proteins are stained by anti-KDEL monoclonals in plants. For comparison, a monoclonal antibody raised to a synthetic HDEL peptide was also used and found to stain a set of proteins in all plant species tested. The anti-HDEL and anti-KDEL monoclonals were sequence specific, staining different proteins. On density gradient fractionation HDEL proteins also banded with ER marker activities. However, the intracellular distribution of HDEL and KDEL proteins determined by immunofluorescence was different. Whereas HDEL proteins showed a distribution characteristic of plant ER, and this localisation was confirmed by immunogold labelling of ultrathin sections and electron microscopy, KDEL proteins showed strong fluorescence in discrete parts of the cell cortex. These observations are discussed in terms of the potential these monoclonal antibodies have as markers for ER and of the role ABP plays in plant cell signalling.

L18 ANSWER 9 OF 299 MEDLINE on STN
ACCESSION NUMBER: 92268110 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1316906
TITLE: Different sorting of Lys-Asp-Glu-Leu proteins in rat liver.
AUTHOR: Peter F; Nguyen Van P; Soling H D
CORPORATE SOURCE: Abteilung Klinische Biochemie, Universitat Gottingen, Federal Republic of Germany.
SOURCE: Journal of biological chemistry, (1992 May 25) 267 (15) 10631-7.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 19920710
Last Updated on STN: 19920710
Entered Medline: 19920625

ED Entered STN: 19920710
Last Updated on STN: 19920710
Entered Medline: 19920625

AB Most of the resident soluble proteins of the endoplasmic reticulum (ER) seem to be sorted into this compartment via their COOH-terminal tetrapeptide Lys-Asp-Glu-Leu (KDEL). This sorting is supposed to occur in a post-ER compartment. Three resident soluble ER glycoproteins belonging to the KDEL family are CaBP1, CaBP2, CaBP3 (= calreticulin), and CaBP4 (= grp94) (Nguyen Van, P., Peter, F., and Soling, H.-D. (1989) J. Biol. Chem. 264, 17494-17501). In rat liver, calreticulin possesses a carbohydrate moiety of the complex hybrid type with terminal galactoses (Nguyen Van, P., Peter, F., and Soling, H.-D. (1989) J. Biol. Chem. 264, 17494-17501). We can show now that practically all calreticulin molecules (and not only a fraction) possess terminal galactoses as well as the COOH-terminal KDEL sequence. This as well as pulse-chase experiments performed at 37 and 15 degrees C indicate that calreticulin must have passed through the trans-Golgi. Subcellular fractionations of post-mitochondrial supernatants from isolated rat hepatocytes by sucrose-Nycodenz gradient centrifugation revealed that calreticulin is confined mainly to the rough ER, grp94 mainly to the smooth ER. CaBP1, a member of the thioredoxin family, was recovered in fractions which most likely represent the intermediate compartment. This indicates that KDEL is a sorting signal which leads to the retention of these proteins in the

pre-Golgi compartments. However, additional factors, most likely residing within the specific KDEL protein itself, determine the final location of the protein within the pre-Golgi compartments. This is underlined by experiments in which the density dependent distribution of total KDEL proteins was studied using a COOH-terminal KDEL-specific antibody.

L18 ANSWER 10 OF 299 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:602708 CAPLUS
DOCUMENT NUMBER: 121:202708
TITLE: A library approach to antibody generation
AUTHOR(S): Gausepohl, H.; Vaux, D.; Fuller, S.; Tooze, J.; Frank, R. W.
CORPORATE SOURCE: ABIMED Analysen-Technik GmbH, Langenfeld, D-4018, Germany
SOURCE: Pept. 1992, Proc. Eur. Pept. Symp., 22nd (1993), Meeting Date 1992, 909-10. Editor(s): Schneider, Conrad H.; Eberle, Alex N. ESCOM: Leiden, Neth. CODEN: 60LUAN
DOCUMENT TYPE: Conference
LANGUAGE: English
ED Entered STN: 29 Oct 1994
AB The endoplasmic reticulum (ER) of living cells contains a series of resident proteins necessary for processing of secreted proteins passing the ER. These proteins contain a C-terminal signal sequence (KDEL) necessary for retention in the ER. To identify and isolate a putative receptor, a library approach was used to generate a pool of antibodies against the C-terminal KDEL sequence. A library of peptide analogs (KXXXXXKDEL) was synthesized. A rabbit antiserum generated against the library was shown to react with a large no. of proteins in a total cell lysate.
IT **113516-56-6DP**, proteins contg.
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(antibodies to; library preparative approach to)

L18 ANSWER 11 OF 299 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:409959 CAPLUS
DOCUMENT NUMBER: 121:9959
TITLE: Synthesis of oligonucleotide-peptide conjugates containing a KDEL signal sequence
AUTHOR(S): Arar, Khali; Monsigny, Michel; Mayer, Roger
CORPORATE SOURCE: Cent. Biophys. Mol., CNRS, Orleans, F-45071, Fr.
SOURCE: Tetrahedron Letters (1993), 34(50), 8087-90 CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 121:9959
ED Entered STN: 09 Jul 1994
AB An improved method of prepn. of oligonucleotide-peptide conjugates is described. An oligopeptide contg. .alpha. and .epsilon.-amino groups is mainly substituted at its .alpha.-NH2 end by .epsilon.-maleimidocaproic acid N-hydroxysuccinimide ester at pH 6.5 for 1 h. The N.alpha.-maleimidocaproyl-peptide deriv., purified by HPLC, reacts with the thiol group of an oligonucleotide at pH 7.2 to give oligonucleotide-peptide conjugate I (Ftc = fluoresceinthiocarbamoyl) in 82% yield. The thiol group is generated in situ by the action of tris(carboxyethyl)phosphine on an oligonucleotide bearing a disulfide bridge.
IT **113516-56-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(signal sequence, synthesis of oligonucleotide-peptide conjugate contg.)

L18 ANSWER 12 OF 299 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:127570 CAPLUS
DOCUMENT NUMBER: 120:127570
TITLE: Pseudomonas exotoxin amino acid substitution and deletion analogs with increased activity
INVENTOR(S): Pastan, Ira H.; Fitzgerald, David J.
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9325690	A1	19931223	WO 1993-US5858	19930617
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9345404	A1	19940104	AU 1993-45404	19930617
AU 675440	B2	19970206		
EP 646175	A1	19950405	EP 1993-915414	19930617
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07508641	T2	19950928	JP 1993-517836	19930617
US 5602095	A	19970211	US 1995-405615	19950315
US 5821238	A	19981013	US 1995-461234	19950605
US 5854044	A	19981229	US 1995-463480	19950605
PRIORITY APPLN. INFO.:			US 1992-901709 A	19920618
			WO 1993-US5858 A	19930617
			US 1995-405615 A3	19950315

ED Entered STN: 19 Mar 1994
AB Analogs of Pseudomonas exotoxin with modifications in domains Ia and II leading to increased toxicity are prepd. for use as therapeutics. The mols. have a deletion of the N-terminal region cleaved during intracellular activation of the protein and a C-terminal anchor domain added with further internal substitutions. The analogs may also be conjugated with cell-targetting ligands such as antibodies, hormones, or cytokines. Genes for a series of deletion analogs and their fusion products with transforming growth factor .alpha. as the C-terminal domain were constructed by std. methods and the genes expressed in Escherichia coli with the expression products recovered from inclusion bodies. All of the products tested showed normal ADP-ribosylation activity with ID50 against A431 cells 0.006-25 ng/mL and they were able to displace bound EGF. Toxicity of the fusion products correlated with the no. of receptor sites/cell.
IT **113516-56-6**
RL: BIOL (Biological study)
(as C-terminal anchor domain in Pseudomonas exotoxin analogs)

L18 ANSWER 13 OF 299 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:597402 CAPLUS
DOCUMENT NUMBER: 119:197402
TITLE: Addition of an endoplasmic reticulum retrieval sequence to ricin A chain significantly increases its cytotoxicity to mammalian cells
AUTHOR(S): Wales, Richard; Roberts, Lynne M.; Lord, J. Michael
CORPORATE SOURCE: Dep. Biol. Sci., Univ. Warwick, Coventry, CV4 7AL, UK
SOURCE: Journal of Biological Chemistry (1993), 268(32), 23986-90
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal

LANGUAGE: English
ED Entered STN: 13 Nov 1993
AB An Escherichia coli expression system was used to produce recombinant ricin A chain (RTA) and RTA modified either by the addn. of a carboxyl-terminal endoplasmic reticulum retrieval sequence Lys-Asp-Glu-Leu (RTAKDEL) or a nonfunctional analog Lys-Asp-Glu-Ala (RTAKDEA). These RTA mols. can enter mammalian cells by fluid phase endocytosis. RTAKDEL was significantly more cytotoxic than either RTA or RTAKDEA to both Vero cells and HeLa cells (250- and 10-fold, resp.), despite the fact that all these RTA mols. had comparable enzymic activities. This difference did not result from KDEL-mediated binding of RTAKDEL to the cell surface. Enhanced cytotoxicity could be correlated with an increased level of ribosome inactivation, measured as the RTA-catalyzed depurination of 28 S rRNA. Thus, the added KDEL sequence facilitated RTA entry into the cytosol. Apparently, interaction with the intracellular KDEL receptor promotes retrograde transport of the toxin to the endoplasmic reticulum, where translocation of RTA into the cytosol occurs.
IT **113516-56-6**
RL: BIOL (Biological study)
(ricin A chain modified by, cytotoxicity of, to mammalian cells)

L18 ANSWER 14 OF 299 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:557969 CAPLUS
DOCUMENT NUMBER: 119:157969
TITLE: Intracellular retention of interleukin-6 abrogates signaling
AUTHOR(S): Rose-John, Stefan; Schooltink, Heidi; Schmitz-Van de Leur, Hildegard; Muellberg, Juergen; Heinrich, Peter C.; Graeve, Lutz
CORPORATE SOURCE: Dep. Biochem., RWTH, Aachen, D-5100, Germany
SOURCE: Journal of Biological Chemistry (1993), 268(29), 22084-91
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 16 Oct 1993
AB Three forms of interleukin-6 (IL-6) have been constructed and stably transfected into human hepatoma cells (HepG2). Wild type IL-6 contg. a signal peptide was rapidly secreted as a biol. active protein. IL-6 lacking the signal peptide accumulated within the cytoplasm of transfected cells. Surprisingly, IL-6 carrying a C-terminal extension of the amino acids Lys-Asp-Glu-Leu (KDEL) was not completely retained in the endoplasmic reticulum (ER). Complete retention in the ER was achieved when the 14 C-terminal amino acids of protein disulfide isomerase which include the KDEL signal were added to the C terminus of IL-6. Thus, the addn. of the protein sorting signal KDEL alone is not sufficient for full retention of IL-6 in the ER. IL-6 accumulated in the cytoplasm and IL-6 retained in the ER failed to induce liver-specific acute-phase protein synthesis in the host cells, indicating that there is no intracellular role of IL-6 in signal transduction. Retention of IL-6 in the ER led to the prevention of surface expression of the IL-6 receptor protein gp80, making these cells unresponsive to IL-6. This phenomenon can be exploited in the future to generate transgenic animals which will become completely cytokine unresponsive in the tissues in which they express an ER retained cytokine.
IT **113516-56-6**
RL: BIOL (Biological study)
(interleukin 6 C terminus extended with, retention within endoplasmic reticulum and signal transduction in relation to)

L18 ANSWER 15 OF 299 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:232146 CAPLUS

DOCUMENT NUMBER: 118:232146
TITLE: Blockade of human immunodeficiency virus type 1 production in CD4+ T cells by an intracellular CD4 expressed under control of the viral long terminal repeat
AUTHOR(S): Buonocore, Linda; Rose, John K.
CORPORATE SOURCE: Sch. Med., Yale Univ., New Haven, CT, 06510, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1993), 90(7), 2695-9
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 Jun 1993
AB A retroviral vector was constructed in which a gene encoding a mutated sol. CD4 protein that is retained in the endoplasmic reticulum (sCD4-KDEL) is expressed under control of human immunodeficiency virus type 1 (HIV-1) regulatory elements. HIV-1 infection of a human T-cell line transduced with this vector led to induction of sCD4-KDEL synthesis and a block in transport of the HIV envelope protein to the cell surface. There was a complete block to maturation of infectious HIV-1 in the transduced cells, no viral spread, and little or no syncytium formation. Infected cells gradually disappeared from the culture over a period of 2 mo. This intracellular trap for HIV has potential application in gene therapy for AIDS.
IT **113516-56-6D**, sol. CD4 antigen contg.
RL: BIOL (Biological study)
(retrovirus vector contg., long terminal repeat-regulated, human immunodeficiency virus replication T-lymphocytes inhibition by)

L18 ANSWER 16 OF 299 MEDLINE on STN
ACCESSION NUMBER: 93321727 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8330633
TITLE: A luminal calcium-binding protein with a KDEL endoplasmic reticulum retention motif in the ER-Golgi intermediate compartment.
AUTHOR: Schweizer A; Peter F; Van P N; Soling H D; Hauri H P
CORPORATE SOURCE: Department of Pharmacology, University of Basel, Switzerland.
SOURCE: European journal of cell biology, (1993 Apr) 60 (2) 366-70.
Journal code: 7906240. ISSN: 0171-9335.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199308
ENTRY DATE: Entered STN: 19930826
Last Updated on STN: 19930826
Entered Medline: 19930819
ED Entered STN: 19930826
Last Updated on STN: 19930826
Entered Medline: 19930819

L18 ANSWER 17 OF 299 MEDLINE on STN
ACCESSION NUMBER: 93216693 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8385108
TITLE: pH-dependent binding of KDEL to its receptor in vitro.
AUTHOR: Wilson D W; Lewis M J; Pelham H R
CORPORATE SOURCE: Medical Research Council Laboratory of Molecular Biology, Cambridge, United Kingdom.
SOURCE: Journal of biological chemistry, (1993 Apr 5) 268 (10) 7465-8.
Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199305
ENTRY DATE: Entered STN: 19930521
Last Updated on STN: 19930521
Entered Medline: 19930505

ED Entered STN: 19930521
Last Updated on STN: 19930521
Entered Medline: 19930505

AB The erd2 protein is the receptor responsible for recycling proteins bearing the carboxyl-terminal sequence KDEL (single-letter amino acid code) to the endoplasmic reticulum, following their loss from that organelle by the process of forward transport. To study the interaction of erd2p with the sequence KDEL we have reconstituted binding of erd2p to its ligand in vitro. Binding in vitro exhibits the same sequence specificity as retention of lumenal proteins in vivo and is strikingly sensitive to pH. Our results raise the possibility that erd2p-mediated sorting of lumenal endoplasmic reticulum proteins is facilitated by the pH differences between compartments of the secretory pathway.

L18 ANSWER 18 OF 299 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:401398 CAPLUS
DOCUMENT NUMBER: 122:210577
TITLE: Cytosolic factors block antibody binding to the C-terminal cytoplasmic tail of the KDEL receptor
AUTHOR(S): Tang, Bor Luen; Wong, Siew Heng; Low, Seng Hui; Subramaniam, V. Nathan; Hong, Wanjin
CORPORATE SOURCE: Institute Molecular and Cell Biology, National University Singapore, Singapore, 0511, Singapore
SOURCE: European Journal of Cell Biology (1994), 65(2), 298-304
CODEN: EJCBDN; ISSN: 0171-9335
DOCUMENT TYPE: Journal
LANGUAGE: English

ED Entered STN: 09 Mar 1995

AB The mammalian KDEL receptor is an extremely hydrophobic membrane protein. One of the longest stretches of hydrophilic sequence resides at the C-terminus. Various antibodies against a synthetic peptide corresponding to this region confirmed that the C-terminus is exposed to the cytoplasm. It was obsd. that antibody binding to the C-terminus of the KDEL receptor was diminished during immunofluorescence microscopy procedures which involved fixation prior to permeabilization as compared to when cells were permeabilized before fixation. Binding of both polyclonal and monoclonal antibodies, as assessed by indirect immunofluorescence microscopy in digitonin permeabilized cells, was inhibited by preincubation with rat liver cytosol. This inhibition was not obsd. with antibody against another membrane protein (p28) with a cytoplasmically exposed epitope also residing in the Golgi/intermediate compartment. Rabbit reticulocyte lysate had a similar effect while Schizosaccharomyces pombe cytosol inhibited binding to a greater degree than Saccharomyces cerevisiae cytosol. This inhibition by cytosol was prevented by coincubation with the antibody and was dose-dependent on the cytosol. Inhibition did not occur on ice or at 15.degree.C, or when the cytosol was energy-depleted by apyrase treatment. Interestingly, pretreatment of permeabilized cells with N-ethylmaleimide or its addn. into the incubation mixt. abolished inhibition. N-ethylmaleimide-treated cytosol, however, remained inhibitory. The findings suggest the existence of cytosolic factor(s) which interacts specifically with the cytoplasmic C-terminus of the KDEL receptor, which are likely to be components of the KDEL protein retrieval machinery.

IT **113516-56-6**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cytosolic factors block antibody binding to the C-terminal cytoplasmic tail of the KDEL receptor)

L18 ANSWER 19 OF 299 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:67090 CAPLUS
DOCUMENT NUMBER: 122:31946
TITLE: Synthesis of peptide-oligonucleotide hybrids containing a KDEL signal sequence
AUTHOR(S): Arar, K.; Monsigny, M.; Mayer, R.
CORPORATE SOURCE: Cent. Biophys. Mol., CNRS, Orleans, F-45071, Fr.
SOURCE: Pept.: Chem., Struct. Biol., Proc. Am. Pept. Symp., 13th (1994), Meeting Date 1993, 184-6. Editor(s): Hodges, Robert S.; Smith, John A. ESCOM: Leiden, Neth.
CODEN: 60LXAW
DOCUMENT TYPE: Conference
LANGUAGE: English
ED Entered STN: 08 Nov 1994
AB A symposium report on the synthesis of peptide-oligonucleotide hybrids contg. a KDEL signal sequence by linking a 3'-thiol oligonucleotide to a N.alpha.-maleimidocaproyl peptide. The oligonucleotide used is a 12-mer with a sequence specific for Ha-ras around the point mutation in the 12th codon. Thus, H-Tyr-Lys-Asp-Glu-Leu-OH was converted into the N.alpha.-maleimidocaproyl deriv., which was treated with 3'-thiol oligonucleotide to give peptide-oligonucleotide hybrid I.
IT **113516-56-6P**
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of peptide-oligonucleotide hybrids contg. a KDEL signal sequence)

L18 ANSWER 20 OF 299 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:697598 CAPLUS
DOCUMENT NUMBER: 121:297598
TITLE: Localization of the Lys, Asp, Glu, Leu tetrapeptide receptor to the Golgi complex and the intermediate compartment in mammalian cells
AUTHOR(S): Griffiths, Gareth; Ericsson, Maria; Krijnse-Locker, Jacomine; Nilsson, Tommy; Goud, Bruno; Soeling, Hans-Dieter; Tang, Bor Luen; Wong, Siew Heng; Hong, Wanjin
CORPORATE SOURCE: European Mol. Biol. Lab., Heidelberg, 69012, Germany
SOURCE: Journal of Cell Biology (1994), 127(6, Pt. 1), 1557-74
CODEN: JCLBA3; ISSN: 0021-9525
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 24 Dec 1994
AB The carboxyl-terminal Lys-Asp-Glu-Leu (KDEL), or a closely-related sequence, is important for endoplasmic reticulum (ER) localization of both lumenal as well as type II membrane proteins. This sequence functions as a retrieval signal at post-ER compartment(s), but the exact compartment(s) where the retrieval occurs remains unresolved. With an affinity-purified antibody against the carboxyl-terminal sequence of the mammalian KDEL receptor, the authors have investigated its subcellular localization using immunogold labeling on thawed cryosections of different tissues, such as mouse spermatids and rat pancreas, as well as HeLa, Vero, NRK, and mouse L cells. The authors show that rab1 is an excellent marker of the intermediate compartment, and the authors use this marker, as well as budding profiles of the mouse hepatitis virus (MHV) in cells infected with this virus, to identify this compartment. The results demonstrate that

the KDEL receptor is concd. in the intermediate compartment, as well as in the Golgi stack. Lower but significant labeling was detected in the rough ER. In general, only small amts. of the receptor were detected on the trans side of the Golgi stack, including the trans-Golgi network (TGN) of normal cells and tissues. However, some stress conditions, such as infection with vaccinia virus or vesicular stomatitis virus, as well as 20.degree. or 43.degree. treatment, resulted in a significant shift of the distribution towards the trans-TGN side of the Golgi stack. This shift could be quantified in HeLa cells stably expressing a TGN marker. No significant labeling was detected in structures distal to the TGN under all conditions tested. After GTP.gamma.S treatment of permeabilized cells, the receptor was detected in the .beta.-coatomer protein-contg. buds/vesicles that accumulate after this treatment, suggesting that these vesicles may transport the receptor between compartments. The authors propose that retrieval of KDEL-contg. proteins occurs at multiple post-ER compartments up to the TGN along the exocytotic pathway, and that within this pathway, the amts. of the receptor in different compartments varies according to physiol. conditions.

IT **113516-56-6**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(KDEL receptor localization to Golgi complex and intermediate compartment)

L18 ANSWER 21 OF 299 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:600051 CAPLUS
DOCUMENT NUMBER: 121:200051
TITLE: Changes in free calcium in the endoplasmic reticulum of living cells detected using targeted aequorin
AUTHOR(S): Kendall, Jonathan M.; Badminton, Michael N.; Dormer, Robert L.; Campbell, Anthony K.
CORPORATE SOURCE: Dep. Med. Biochemistry, Univ. Wales Coll. Med., Heath Park/Cardiff, CF4 4XN, UK
SOURCE: Analytical Biochemistry (1994), 221(1), 173-81
CODEN: ANBCA2; ISSN: 0003-2697
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 29 Oct 1994
AB The Ca2+-activated photoprotein aequorin has been engineered with the endoplasmic reticulum (ER)-targeting sequence from calreticulin at the N-terminus and the KDEL sequence at the C-terminus so that it locates in the ER of living cells. Targeting of apoaequorin to the ER of COS7 cells was demonstrated by immunolocalization. Selective permeabilization of cells expressing the modified protein suggested that targeting was highly efficient. Functional photoprotein was reconstituted in live cells by incubating them with coelenterazine. Light emission from cells expressing ER aequorin showed that the estd. free Ca2+ within the ER of live cells at 37.degree. was 0.3-1.0 .mu.M, some 10 times that in the cytosol. An increase in the rate const. for aequorin light emission was demonstrated when the cells were warmed from 4.degree.. This increase could be in part, but not wholly, explained by an increase in rate consts. for aequorin at higher temps. and a change in kinetics as a result of the ER targeting of aequorin. The increase in rate consts. in the cells was inhibited by thapsigargin and occurred in the presence or absence of extracellular Ca2+. These results highlight the importance of converting aequorin light emission to rate consts. and of calibrating any variants if qual. and quant. conclusions are to be drawn about free Ca2+ in intracellular compartments.

IT **113516-56-6**
RL: ANST (Analytical study)
(at carboxy-terminus of endoplasmic reticulum-targeting recombinant aequorin, detection of changes in free calcium in ER in relation to)

L18 ANSWER 22 OF 299 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:532202 CAPLUS
DOCUMENT NUMBER: 121:132202
TITLE: Immunomodulatory peptides
INVENTOR(S): Urban, Robert Glen; Chicz, Roman M.; Vignali, Dario A.; Hedley, Mary Lynne; Stern, Lawrence J.; Strominger, Jack L.
PATENT ASSIGNEE(S): Harvard College, USA
SOURCE: PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9404171	A1	19940303	WO 1993-US7545	19930811
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6696061	B1	20040224	US 1993-77255	19930615
EP 671926	A1	19950920	EP 1993-921177	19930811
EP 671926	B1	20021113		
R: DE, FR, GB, IT				
JP 08504177	T2	19960507	JP 1993-506377	19930811
JP 3491896	B2	20040126	JP 1994-506377	19930811
PRIORITY APPLN. INFO.:			US 1992-925460 A	19920811
			US 1993-77255	19930615
			WO 1993-US7545 W	19930811

ED Entered STN: 17 Sep 1994
AB A purified prepn. of a peptide consisting essentially of an amino acid sequence identical to that of a segment of a naturally-occurring human protein, said segment being of 10 to 30 residues in length, inclusive, wherein said peptide binds to a human major histocompatibility complex (MHC) class II allotype. The naturally-occurring human protein is selected from HLA-A2, HLA-A29, HLA-A30, HLA-B44, HLA-DR, K+ channel protein, CD45, vinculin, acetylcholine receptor, etc. Methods for making and identifying the immunomodulary peptides are disclosed, and liposome contg. and nucleic acid encoding such peptide are also claimed.
IT **113516-56-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(peptide immunomodulator)

L18 ANSWER 23 OF 299 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:407323 CAPLUS
DOCUMENT NUMBER: 121:7323
TITLE: Immunomodulatory peptides binding to human major histocompatibility complex (MHC) class II allotype
INVENTOR(S): Urban, Robert Glen; Chicz, Roman M.; Vignali, Dario A. A.; Hedley, Mary Lynne; Stern, Lawrence J.; Strominger, Jack L.
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9404557	A1	19940303	WO 1992-US6692		19920811
W: JP					
JP 08502244	T2	19960312	JP 1994-506181		19920811
JP 2003289887	A2	20031014	JP 2003-35576		19920811
PRIORITY APPLN. INFO.:			JP 1994-506181	A	19920811
			WO 1992-US6692	W	19920811

ED Entered STN: 09 Jul 1994

AB A purified oligopeptide prepn. comprising an amino acid sequence identical to that of a segment of a naturally-occurring human protein that binds to human major histocompatibility complex (MHC) class II allotype is provided. The human protein is an MHC class I or II mol., HLA-A2, invariant chain (Ii), etc.,. A method is described for inhibiting an immune response in a human patient by contacting an antigen-presenting cell (APC) of the patient with a therapeutic compn. or an immune-stimulating complex (ISCOM) contg. the oligopeptide, or by expression of the oligopeptide-coding sequence linked to a trafficking sequence in APCs. The oligopeptide also can be used for inducing an immune response against pathogens. The options of the oligopeptide delivery system is also described. Purifn. and characterization of 6 HLA-DR antigens (HLA-DR1.apprx.4; HLA-DR7.apprx.8) from Epstein-Barr virus-transformed human B lymphoblastoid cell lines were demonstrated.

IT **113516-56-6**
RL: BIOL (Biological study)
(intracellular trafficking sequence, delivery of MHC class II allotype-binding peptides in relation to)

L18 ANSWER 24 OF 299 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1994:263046 CAPLUS
DOCUMENT NUMBER:	120:263046
TITLE:	Method of intracellular binding of target molecules
INVENTOR(S):	Marasco, Wayne A.; Haseltine, William A.
PATENT ASSIGNEE(S):	Dana-Farber Cancer Institute, USA
SOURCE:	PCT Int. Appl., 154 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9402610	A1	19940203	WO 1993-US6735		19930716
W: AU, CA, JP, US					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
EP 651805	A1	19950510	EP 1993-918231		19930716
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
JP 09501821	T2	19970225	JP 1993-504609		19930716
AU 687010	B2	19980219	AU 1993-47753		19930716
AU 9347753	A1	19940214			
CN 1084216	A	19940323	CN 1993-116556		19930717
US 6004940	A	19991221	US 1994-350215		19941206
US 5851829	A	19981222	US 1995-373190		19950330
US 5965371	A	19991012	US 1995-438190		19950509
US 6072036	A	20000606	US 1999-287145		19990406
US 6329173	B1	20011211	US 2000-556111		20000421
PRIORITY APPLN. INFO.:			US 1992-916939	A	19920717
			US 1993-45274	A	19930317
			WO 1993-US6735	W	19930716
			US 1995-438190	A3	19950509
			US 1999-287145	A3	19990406

ED Entered STN: 28 May 1994

AB The present invention relates to a method by which one can disrupt

function of an undesired target mol. or target antigen, preferably a protein. The method comprises the intracellular expression of an antibody capable of binding to the target. A DNA sequence, which codes for the portion of an antibody capable of binding to the target operably linked to a promoter that will permit expression of the antibody in the cell(s) of interest, is delivered to a cell. The antibody is then expressed intracellularly and binds to the target, thereby disrupting the target from its normal actions. A vector for an anti-HIV-1 gp120 single-chain antibody fused to endoplasmic reticulum localization peptide KDEL was prepd. COS-1 cells and COS-1 cells constitutively expressing this vector were infected with HIV-1. Viral replication was delayed and infectious viral titer was decreased in the cells contg. the vector. A 80-90% decrease in syncytium formation was also obsd.

IT **113516-56-6**
RL: USES (Uses)
(endoplasmic reticulum localization peptide, intracellular antigen-binding antibodies or antibody fragments contg., vectors encoding)

L18 ANSWER 25 OF 299 MEDLINE on STN
ACCESSION NUMBER: 95002986 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7919379
TITLE: Autocrine stimulation by erythropoietin (Epo) requires Epo secretion.
AUTHOR: Villeval J L; Mitjavila M T; Dusanter-Fourt I; Wendling F; Mayeux P; Vainchenker W
CORPORATE SOURCE: INSERM U.362, Institut Gustave Roussy, Villejuif, France.
SOURCE: Blood, (1994 Oct 15) 84 (8) 2649-62.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199411
ENTRY DATE: Entered STN: 19941222
Last Updated on STN: 19941222
Entered Medline: 19941109

ED Entered STN: 19941222
Last Updated on STN: 19941222
Entered Medline: 19941109

AB Erythropoietin (Epo) autocrine stimulation has been implicated in erythroblastic leukemia. To examine whether this stimulation could occur intracellularly, we developed Epo autocrine models of stimulation in the human pluripotent UT-7 cell line. Retroviral expression of Epo totally abolished the growth factor requirement of UT-7 cells. Autonomous proliferation was not cell density-dependent and occurred at a unicellular level, showing a genuine autocrine mode of stimulation. Total blockage of Epo secretion induced by the endoplasmic reticulum-retention amino acids Lys-Asp-Glu-Leu (KDEL) signals in 11 lines prevented autonomous proliferation, whereas a leaky retention system, observed in 3 other lines, resulted in limited autocrine stimulation without true long-term autonomous proliferation. Production of Epo, in contrast to KDEL-modified Epo, induced reductions in Epo binding, Epo receptor (EpoR) mRNA, and phosphorylation levels similar to those induced by the addition of exogenous Epo to the parental cell line. In addition, autonomous growth and survival were inhibited by the addition of Epo-neutralizing antibodies, affording evidence that autocrine stimulation through EpoR activation takes place on the cell surface. Finally, phenotypic analysis of the virus-infected clones indicated that Epo production did not change the differentiative capacities of UT-7 cells. All these data show that Epo autocrine stimulation is dependent on Epo secretion and takes place on the cell surface. From all analyzed parameters, the effects of Epo

autocrine stimulation and those of exogenously added Epo appear to be identical.

L18 ANSWER 26 OF 299 MEDLINE on STN
ACCESSION NUMBER: 94357273 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8076688
TITLE: Posttranslational processing of a carboxy-terminal propeptide containing a KDEL sequence of plant vacuolar cysteine endopeptidase (SH-EP).
COMMENT: Erratum in: FEBS Lett 1994 Dec 12;356(1):152
AUTHOR: Okamoto T; Nakayama H; Seta K; Isobe T; Minamikawa T
CORPORATE SOURCE: Department of Biology, Tokyo Metropolitan University, Japan.
SOURCE: FEBS letters, (1994 Aug 29) 351 (1) 31-4.
Journal code: 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199410
ENTRY DATE: Entered STN: 19941013
Last Updated on STN: 20000303
Entered Medline: 19941003
ED Entered STN: 19941013
Last Updated on STN: 20000303
Entered Medline: 19941003
AB A plant cysteine endopeptidase, designated SH-EP, is a major protease occurring in cotyledons of Vigna mungo seedlings, and acts to degrade seed globulin stored in protein bodies. Here we show that the 43 kDa intermediate of SH-EP formed in the endoplasmic reticulum is transported to protein bodies and processed to the 33 kDa mature form during transport or thereafter, and that the COOH-terminal propeptide of 10 amino acid residues containing a KDEL sequence, which is known as a retention signal for the endoplasmic reticulum lumen, is processed to form the mature SH-EP.

L18 ANSWER 27 OF 299 TOXCENTER COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:166651 TOXCENTER
COPYRIGHT: Copyright 2004 ACS
DOCUMENT NUMBER: CA12111132202U
TITLE: Immunomodulatory peptides
AUTHOR(S): Urban, Robert Glen; Chicz, Roman M.; Vignali, Dario A.; Hedley, Mary Lynne; Stern, Lawrence J.; Strominger, Jack L.
CORPORATE SOURCE: ASSIGNEE: Harvard College
PATENT INFORMATION: WO 944171 A1 3 Mar 1994
SOURCE: (1994) PCT Int. Appl., 139 pp.
CODEN: PIXXD2.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1994:532202
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20020910
ED Entered STN: 20011116
Last Updated on STN: 20020910
AB A purified prepn. of a peptide consisting essentially of an amino acid sequence identical to that of a segment of a naturally-occurring human protein, said segment being of 10 to 30 residues in length, inclusive, wherein said peptide binds to a human major histocompatibility complex (MHC) class II allotype. The naturally-occurring human protein is

selected from HLA-A2, HLA-A29, HLA-A30, HLA-B44, HLA-DR, K+ channel protein, CD45, vinculin, acetylcholine receptor, etc. Methods for making and identifying the immunomodulary peptides are disclosed, and liposome contg. and nucleic acid encoding such peptide are also claimed.

L18 ANSWER 28 OF 299 MEDLINE on STN
ACCESSION NUMBER: 1999034887 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9816055
TITLE: Immunotoxins that target an oncogenic mutant epidermal growth factor receptor expressed in human tumors.
AUTHOR: Lorimer I A; Wikstrand C J; Batra S K; Bigner D D; Pastan I
CORPORATE SOURCE: Laboratory of Molecular Biology, Division of Cancer Biology, National Cancer Institute, NIH, Bethesda, Maryland 20892, USA.
SOURCE: Clinical cancer research : an official journal of the American Association for Cancer Research, (1995 Aug) 1 (8) 859-64.
Journal code: 9502500. ISSN: 1078-0432.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990301
Last Updated on STN: 20000303
Entered Medline: 19990218
ED Entered STN: 19990301
Last Updated on STN: 20000303
Entered Medline: 19990218
AB Human cancers arise from a series of mutations, many of which direct the expression of mutant proteins with altered functions. These aberrant proteins are attractive targets for new therapeutic agents. One such protein is a mutant epidermal growth factor receptor (EGFRvIII) that has an in-frame deletion near the NH2 terminus of its extracellular domain. This protein was first identified in human gliomas, but has also been shown to be present in lung and breast carcinomas. The deletion results in a receptor with constitutive tyrosine kinase activity that enhances the tumorigenicity of glioblastomas in vivo. The deletion also creates a tumor-specific cell-surface sequence at the deletion junction. Three specific anti-EGFRvIII mAbs have been isolated following immunization with a mixture of a deletion junction synthetic peptide and EGFRvIII as present on cell membranes. We have constructed immunotoxins by conjugating a modified version of Pseudomonas exotoxin A to these mAbs. Immunotoxins were tested on cells that had been transfected with cDNA for the EGFRvIII receptor and expressed receptor protein at 5 x 10(5) receptors/cell. All three immunotoxins were cytotoxic to these cells, with 50% inhibition of protein synthesis occurring in a 15-50 pM range. The immunotoxins specifically targeted EGFRvIII, as their cytotoxicity could be blocked by their respective free antibody. They showed little or no cytotoxicity to cells expressing high levels of normal epidermal growth factor receptors, demonstrating that they are able to discriminate between cells expressing the mutant receptor and those expressing the wild-type receptor. Immunotoxins targeted to mutant epidermal growth factor receptors are promising candidates for further development as tumor cell-specific therapeutic agents.

L18 ANSWER 29 OF 299 MEDLINE on STN
ACCESSION NUMBER: 96113596 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8974463
TITLE: Generation of a potent chimeric toxin by replacement of domain III of Pseudomonas exotoxin with ricin A chain KDEL.
AUTHOR: Pitcher C; Roberts L; Fawell S; Zdanovsky A G; FitzGerald D

J; Lord J M
CORPORATE SOURCE: Department of Biological Sciences, University of Warwick, Coventry, U.K.
SOURCE: Bioconjugate chemistry, (1995 Sep-Oct) 6 (5) 624-9. Journal code: 9010319. ISSN: 1043-1802.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 20020420
Entered Medline: 19961227
ED Entered STN: 19970128
Last Updated on STN: 20020420
Entered Medline: 19961227
AB Following cellular uptake, Pseudomonas exotoxin (PE) is cleaved by cellular protease which generates an enzymatically active C-terminal fragment (amino acids 280-613). This 37 kD fragment translocates to the cell cytosol where it ADP-ribosylates elongation factor 2 and inhibits protein synthesis. A recombinant hybrid toxin (designated PE-RTA) in which the ADP-ribosylation domain (domain 111) was replaced by the RNA N-glycosidase domain of ricin (the A chain or RTA) has been produced in E. coli. The hybrid toxin effectively and specifically depurinated 28S ribosomal RNA, indicating that the ricin A moiety folded into its native conformation. The cytotoxicity of PE-RTA for L929 cells was approximately 100-fold less than either native PE or whole ricin. However, the addition of the tetrapeptide KDEL to the C-terminus of PE-RTA (producing PE-RTA KDEL) increased cytotoxicity to the level of the native toxins. By analogy to PE, both PE-RTA and PE-RTA KDEL would be proteolytically cleaved within PE domain II during cell entry. A single amino acid substitution, believed to disrupt an essential step in the transport of the catalytically active PE fragment to the cell cytosol (Trp281 to Ala: Zdanovsky, A.G., Chiron, M., Pastan, I., and FitzGerald, D. J. (1993) J. Biol. Chem. 268, 21791-21799), reduced the cytotoxicities of both PE and PE-RTA KDEL by approximately 100-fold. Taken together, these data show that the ricin A chain component of the hybrid toxin requires essential PE-derived sequences at both the N- and C-termini of the translocating fragment. Clearly, in the context of this fusion protein, ricin A chain cannot effect its own transfer to the cytosol.

L18 ANSWER 30 OF 299 MEDLINE on STN
ACCESSION NUMBER: 96113589 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8974456
TITLE: Synthesis and antiviral activity of peptide-oligonucleotide conjugates prepared by using N alpha-(bromoacetyl)peptides.
AUTHOR: Arar K; Aubertin A M; Roche A C; Monsigny M; Mayer R
CORPORATE SOURCE: Laboratoire de Biochimie des Glycoconjugues, CNRS, Orleans, France.
SOURCE: Bioconjugate chemistry, (1995 Sep-Oct) 6 (5) 573-7. Journal code: 9010319. ISSN: 1043-1802.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961227
ED Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961227

AB Antisense oligonucleotides represent an interesting tool for selective inhibition of gene expression. In order to direct oligonucleotides to specific compartments within the cell, we have investigated the possibility of coupling them to a signal peptide Lys-Asp-Glu-Leu (KDEL). This sequence should be able to convey oligonucleotides to the endoplasmic reticulum and from there to the cytosol and the nucleus where their targets are located. On this basis we prepared peptide-oligonucleotide conjugates by coupling, in a single step, a Nalpha-bromoacetyl peptide with an oligonucleotide bearing a thiol group, through a thioether bond. This paper deals with the definition of the optimal pH and temperature conditions leading to an efficient synthesis of peptide-oligonucleotide conjugates: the reaction was quantitative at pH 7.5 within few hours. This method was first set up using a 5',3'-modified dodecanucleotide and a (bromoacetyl)pentapeptide as a conjugation model. Then a 5',3'-modified pentacosanucleotide, complementary to the translation initiation region of the gag mRNA of HIV, was coupled to a (bromoacetyl)dodecapeptide containing a KDEL signal sequence. The anti-HIV activity of the pentacosanucleotide was compared with that of pentacosanucleotide-dodecapeptide conjugates linked through either a thioether bond or a disulfide bridge. The conjugate with a thioether bond has a higher antiviral activity than the peptide-free oligonucleotide and the conjugate linked via a disulfide bond.

FILE 'HOME' ENTERED AT 13:04:36 ON 09 AUG 2004